REMARKS

Claims 38-68 are pending and under examination. Claims 38-43 and 58 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 38-43 can be found in the original claims and merely incorporates language from the preamble into the body of the claim. Support for the amendment to claim 39 for administering cells expressing one or more heterologous epitopes to an individual can be found, for example, on page 59, lines 5-9. The amendment to claim 58 merely corrects a typographical error. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Please note that Applicant submits herewith a replacement Declaration with original signature to replace the Declaration filed as Exhibit 1 on July 29, 2003, which was signed electronically. These Declarations are identical in content.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 38, 41 and 42 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicant respectfully maintains that the specification provides sufficient description and guidance to enable the claimed methods.

Applicant respectfully maintains, for the reasons of record, that the specification provides sufficient description and guidance for various routes of administration. With regard to targeting lymphoid tissues other than spleen, Applicant respectfully maintains that the Rule 132 Declaration by Dr. Zanetti filed in the response submitted July 29, 2003, corroborates Applicant's position. The Declaration indicates that a large percentage of the cells in various lymphoid tissues are B cells, including 10-15% in peripheral blood, 40-50% in spleen, 20-25% in lymph nodes, and 60-70% in Payer's patches. Based on the presence of a large percentage of B cells in various lymphoid tissues, Applicant respectfully maintains that the expression in B cells exemplified by administration to spleen is enabling for administration to various lymphoid tissues, as attested to by Dr. Zanetti in the previously filed Declaration. Therefore, Applicant respectfully maintains that the specification, in combination with what was well known to those skilled in the art, provides sufficient description and guidance to enable the claimed methods.

Applicant respectfully maintains that the reference by Maloy et al., Proc. Natl. Acad. Sci. USA 98:3299-3203 (2001), which was submitted as Exhibit 2 with the response filed July 29, 2003, corroborates Applicant's position that administration to various lymphoid tissues is enabled by the teachings in the specification. Maloy et al. clearly demonstrates that administration of a nucleic acid vector to lymph nodes resulted in efficient expression of antigen and enhanced immunogenicity. Maloy et al. indicates on page 3303, last paragraph, that:

> immunization directly into organized lymphoid tissues with a plasmid DNA vaccine elicited antiviral immunity that was qualitatively and quantitatively superior to what could be achieved by conventional inoculation routes and suggest that i.ln. [intra-lymph node] administration could be a potent means of optimizing the immunogenicity of DNA vaccines. In humans, injection into a s.c. lymph node is readily feasible with the use of ultrasound guidance and is a simple procedure that takes only a few minutes.

The Office Action acknowledges that Maloy et al. does not utilize a B cell specific promoter. In the absence of using a B cell specific promoter, it is not surprising that the "superior" immunity observed by Maloy et al. would result from the normal function of dendritic cells as antigen presenting cells. Based on the description in Maloy et al. of superior immunity obtained by intra-lymph node injection, the utilization of a B cell promoter as taught in Applicant's specification and recited in the claims, and the presence of 20-25% B cells in lymph nodes, one skilled in the art would have had a reasonable expectation of successfully stimulating an immune response using the claimed methods.

With respect to the references by Deonarian, Exp. Opin. Ther. Patents 8:53-69 (1998), and Miller et al., FASEB J. 9:190-199 (1995), referred to in the Office Action, Applicant maintains, for the reasons of record, that unpredictability is not an issue with respect to the claimed methods. Applicant respectfully maintains any unpredictability for *in vivo* targeting and expressing genes as described in these general review articles is not applicable to the claimed invention because the claims explicitly recite that the heterologous epitopes are expressed in a B cell and are, therefore, directed to methods where the nucleic acids have been successfully targeted to a B cell and expressed by a B cell.

Applicant maintains that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 38-43 and 58-68 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Claims 38-43 are indicated to lack a method step resulting in the recited use in the preamble. Applicant respectfully maintains that the claims are clear and definite. Nevertheless, to further prosecution, claims 38-43 have been amended as suggested by the Examiner to incorporate language from the preamble into the body of the claim. Therefore, it is respectfully requested that this rejection be withdrawn.

Claim 39 is alleged to be indefinite because it is unclear how an immune response is generated. Claim 39 has been amended to explicitly recite administering cells expressing one or more heterologous epitopes to an individual. Applicant respectfully submits that claim 39 is clear and definite and requests that this rejection be withdrawn.

Claim 58 is alleged to be indefinite because it does not further limit claim 55, from which it depends. Claim 58 has been amended to depend from claim 57. Accordingly, claim 58 and its dependent claims 59-68 are clear and definite, and it is respectfully requested that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claims 40, 43 and 45-68 under 35 U.S.C. § 103 as allegedly obvious over Soo Hoo, U.S. Patent No. 5,891,432, in view of Banerji et al., Cell 33:729-740 (1983), is respectfully traversed. Applicant respectfully submits that these claims are unobvious over Soo Hoo, alone or in combination with Banerji et al.

Applicant respectfully submits that there would have been no motivation to combine the teachings of Soo Hoo with those of Banerji et al. The Office Action indicates that Soo Hoo describes using myeloma or plasmacytoma cells, referencing column 19-22 and 49-50, claims 13-24. However, there appears to be no reference to myeloma in Soo Hoo.

The Office Action indicates that Soo Hoo does not describe using B cell expression elements in the plasmid vectors. Furthermore, Applicant respectfully submits that there is no teaching or suggestion in Soo Hoo that would have motivated one skilled in the art to combine these teachings with those of Banerji et al. and use a B cell expression element, absent Applicant's teachings. Applicant submits that the mere mention of a plasmacytoma cell would in no way provide motivation for one skilled in the art to use the B cell expression element described in Banerji et al.

It is well settled that Applicant's disclosure cannot be used to hunt through the prior art for the claimed elements and then combine them as claimed (In re Laskowski, 871 F. 2d 115, 117, 10 USPQ 2d 1397, 1398 (Fed. Cir. 1989). Hindsight cannot be used to resolve the question of obviousness (Orthopedic Equipment Co., Inc. v United States, 702 F.2d 1005, 1012 (Fed. Cir. 1983)):

> [t]he difficulty which attaches to all honest attempts to answer this question [non-obviousness] can be attributed to the strong temptation to rely on hindsight while undertaking this evaluation. It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.

It is respectfully submitted that the only way the disclosures of Soo Hoo and Banerji et al. can be read to result in the instantly claimed methods and compositions is with benefit of Applicant's disclosure. Such hindsight application of Applicant's disclosure is clearly improper.

Applicant points out that claims 40 and 43 are directed to *ex vivo* methods. It is further pointed out that a text search of Soo Hoo reveals that the term "*ex vivo*" is not recited in this reference. Furthermore, there is no teaching or suggestion in Banerji et al. of *ex vivo* administration to stimulate an immune response.

Applicant maintains that there is no motivation to combine the teachings of Soo Hoo with the teachings of Banerji et al. to obtain the claimed methods and compositions, absent the teachings in Applicant's specification. Therefore, it is respectfully submitted that the claimed methods are unobvious over Soo Hoo, alone or in combination with Banerji et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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